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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,795	07/09/2003	Andrew J. Dannenberg	CRF D-2756 NB	8535

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EXAMINER	
ROBERTS, LEZAH	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
06/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/614,795	DANNENBERG ET AL.	
	Examiner	Art Unit	
	LEZAH W. ROBERTS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Election of Species response filed December 6, 2007. All rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's election without traverse of the species of oral premalignant lesion of the tongue in the reply filed on December 6, 2007 is acknowledged.

Claims 7-9 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 6, 2007.

Claims

Claim Rejections - 35 USC § 103 – Obviousness (New Rejection)

1) Claims 6 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seibert et al. (US 5,972,986) in view of Jaradat et al. (Biochemical Pharmacology 2001) and Mestre et al. (Annals of the New York Academy of Sciences 1999).

Seibert et al. disclose cyclooxygenase-2 inhibitors or derivatives thereof treat neoplasia. Prostaglandins play a major role in the inflammation process and the inhibition of prostaglandin production especially production of PGG2, PGH2 and PGE

has been a common target of anti-inflammatory drugs discovery. COX-2 is a viable target of inhibition which more reduces inflammation and produces fewer and less drastic side effects. COX-2 has been observed in neoplastic disease. Neoplasia includes both benign and cancerous tumours, growths and polyps. The neoplasia that produce prostaglandins include brain cancer, epithelial cell-derived neoplasia (epithelial carcinoma) such as basal cell carcinoma, adenocarcinoma, gastrointestinal cancer such as lip cancer, mouth cancer, esophogeal cancer, small bowel cancer and stomach cancer, colon cancer, ovary cancer, cervical cancer, lung cancer, breast cancer and skin cancer, such as squamous cell and basal cell cancers, prostate cancer, renal cell carcinoma, and other known cancers that effect epithelial cells throughout the body. The method can be used to treat subjects having adenomatous polyps, including those with familial adenomatous polyposis (FAP). Additionally, the method can be used to prevent polyps from forming in patients at risk of FAP. Inhibitors of the cyclooxygenase pathway in the metabolism of arachidonic acid used in the prevention and treatment of epithelial cell derived neoplasias may inhibit enzyme activity through a variety of mechanisms. By the way of example, the inhibitors used in the methods described herein may block the enzyme activity directly by acting as a substrate for the enzyme.

The reference differs from the instant claims insofar as it does not disclose the COX-2 selective inhibitors were screened using the process recited in the instant claims.

Jaradat et al. disclose activation of peroxisome proliferator-activated receptor (PPAR) isoforms. PPAR isoforms play a role in the regulation of inflammatory

processes in the body. PPAR gamma activation inhibits the induction of PGHS-2. PHGS-2 and may be the target of NSAIDS acting in their anti-inflammatory capacities. In order to screen for PPAR activation, peroxisome proliferator response element-luciferase reporter is used. The data is then normalized to percent response of control cells for PPAR gamma.

In regards to the limitation of luciferase activity data being normalized with beta-galactosidase activity, this is a method disclosed by the art[1] and therefore it would have been obvious to use this method when determining luciferase activity. The reference differs from the instant claims insofar as it does not disclose the compositions being tested are selective inhibitors of COX-2 to test for the likelihood of success for treating cancer.

Mestre et al. disclose COX-2 is important in carcinogenesis. Epidermal growth factor mediates activation of COX-2 expression. COX-2 is unregulated in transformed cells and in malignant tissue. Deregulated signaling through the epidermal growth factor receptor (EGFR) pathway is an early event in the development of head and neck cancers and may contribute to the over expression of COX-2 in HNSCC. Treatment with EGF led to approximately a 100% increase in production of PGE_2. Enhanced synthesis of PG, a consequence of upregulation of COX-2, can increase cell proliferation, promote angiogenesis and inhibit immune surveillance. Compounds were tested to determine if they would suppress EGF-mediated induction of COX-2 in cultured oral squamous carcinoma cells. It was seen that these compounds suppressed

EGF-mediated induction of COX-2. These compounds are also disclosed to down regulate EGFR and transforming growth factor alpha, inhibits cellular proliferation, and induces apoptosis (page 69, second paragraph).

In regards to the degree of down regulation of expression of Class I family of receptors tyrosine kinase, Normally, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find workable conditions generally involves the application of no more than routine skill in the art. In re Aller 105 USPQ 233, 235 (CCPA 1955). It would have been obvious to obtain a certain amount of down regulation in order more obtain a more effective drug candidate. The reference differs from the instant claims insofar as it does not disclose the compositions being tested are selective inhibitors of COX-2 to test for the likelihood of success for treating cancer.

Overexpression of COX-2 has been disclosed to be associated with different cancers. The primary reference has discloses the inhibitions of COX-2 expression may be performed by several mechanisms. Different ways of determining COX-2 inhibition includes those of the secondary references such as testing for PPAR activation by monitoring PPRE-luciferase activation and testing a compound for its effect on EGF-mediated induction of COX-2 to determine their activity on COX-2 and COX-2 synthesis of prostaglandins. It may be concluded that down regulation of EGF would down regulate COX-2. Since prostaglandins play a role in cancer and COX-2 is overexpressed in cancers such as oral cancers, it would have been obvious to screen

[1] Liang et al., FEBS Letters, Volume 496, Issue 1, May 2001, Pages 12 – 18. See page 94 col. 2,

inhibitors of COX-2 for the likelihood of success to treat cancer using these methods motivated by desire to use screening methods that are used to determine a compounds effect on COX-2 regulation as disclosed by the prior art.

Claims 6 and 10 are rejected.

Claims 7-9 and 11 are withdrawn.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LEZAH W. ROBERTS whose telephone number is (571)272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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paragraph 3.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lezah W Roberts/

Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612